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TITLE: Predicting Prostate Cancer Recurrence by Gene Expression Analysis of Formalin-Fixed, Paraffin Embedded Tissue

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14. ABSTRACT
Prostate cancer is the leading cancer diagnosed in men and accounts for approximately 30,000 deaths per year in the US, with large racial disparities in outcome. In additional to racial differences in outcome, factors affecting prognosis include clinical stage, Gleason grade, and PSA levels. The genetic contribution to prostate cancer risk is well accepted, but less has been done to evaluate the genetic contribution to recurrence risk and variation by race. With the advent of newer technologies, discovery of molecular signatures of prognosis is now possible and is the focus of this study. Using a new application, Illumina's DASL assay, we are evaluating approximately 500 genes for expression differences comparing men with and without recurrence. The gene expression sets for African American men will be compared to those for white men to identify genes contributing to racial disparities in outcome. A unique and diverse patient population has been identified and biospecimens processed for gene expression studies of prostate cancer recurrence and racial disparities in outcome. From the eligible study population, RNA has been isolated from 608 tumor samples. This work has taken the first year of the grant to complete. Next steps include finalization of the genes to be included on the expression array and conducting the expression analysis.

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Prostate Cancer, Race, Gene Expression

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Introduction: Prostate cancer is the leading cancer diagnosed in men, accounting for approximately 27,000 deaths in 2007 in the US (1). Large racial disparities in outcome are seen, with African American men having poorer survival after a diagnosis than white men (2). In addition to racial differences in outcome (both recurrence and overall survival), factors affecting prognosis include clinical stage, Gleason grade, and PSA levels (2, 3). The genetic contribution to prostate cancer risk is well accepted, but less has been done to evaluate the genetic contribution to recurrence risk and variation by race. With the advent of newer technologies, discovery of molecular signatures of prognosis is now possible and is the focus of this study. Using a new application, Illumina's DASL assay, we are evaluating approximately 500 genes for expression differences comparing men with and without recurrence. The gene expression sets for African American men will be compared to those for white men to identify genes contributing to racial disparities in outcome.

Body: The study population for the proposed work includes men diagnosed with prostate cancer and undergoing radical prostatectomies for clinically localized prostate cancer from January 1991 through June 1996. Approximately 750 men (330 African American and 420 white) had sufficient follow-up and tumor blocks for initial inclusion. These men also have data available on age, family history, clinical stage, preoperative Gleason score and PSA, preoperative hormonal therapy, and post-operative stage, nodal status, Gleason score, capsular, margin, or seminal vesicle involvement, tumor volume, treatments, PSA. Long-term survival data are also available.

From the eligible study population, RNA has been isolated from 608 tumor samples. Eleven samples do not yet have RNA extracted, 27 samples have too little tissue for successful RNA extraction, and 66 have only normal tissue available. This work has taken the first year of the grant to complete.

The next steps will be to review the panel of genes proposed so that newly identified regions associated with prostate cancer recurrence and/or racial disparities can be included on the panel.

Because Dr. Everson, the PI on the award, left Wayne State University in October of 2006 and did not make arrangements to move this grant or continue this work, no progress was made between October 2006 and October 2007. We have submitted a request to change PI so that this important work can continue. We have also submitted a new IRB application with a change in PI.

Key Research Accomplishments:

- A unique and diverse patient population has been identified.
- 608 biospecimens with usable RNA were processed for gene expression studies of prostate cancer recurrence and racial disparities in outcome.
- Submission of a new IRB application with a change in PI.

Reportable Outcomes: Development of RNA repository for gene expression studies.

Conclusion: Progress has been made in meeting the stated goals of this study, with the development of a biorepository of RNA from a racially diverse population of men with localized prostate cancer. However, continued progress is stalled because the PI left the contracting institution without plans for ensuring that this work continues. Continuing this important work will require a change in PI.

References:

1. Jemal A, Siegel R, Ward E, et al. Cancer Statistics, 2007. CA Cancer J Clin 2003; 57:43-66.

2. Powell IJ, Heilbrun LK, Sakr W, et al. The predictive value of race as a clinical prognostic factor among patients with clinically localized prostate cancer: a multivariate analysis of positive surgical margins. Urology 1997; 49:726-31.
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Appendices: NA